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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/570,594	10/31/2006	Chikako Takatoh	TAKATOH1	2977

1444 7590 11/21/2008

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EXAMINER	
PANDE, SUCHIRA	
ART UNIT	PAPER NUMBER
1637	
MAIL DATE	DELIVERY MODE
11/21/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/570,594	TAKATOH ET AL.	
	Examiner	Art Unit	
	SUCHIRA PANDE	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4 and 6-8* is/are pending in the application.

4a) Of the above claim(s) *8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4 and 6-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 10, 2008 has been entered.

Claim Status

2. Applicant has amended claim 4 and cancelled claim 5. Claims 4, 6-8 are pending. Claim 8 drawn to an apparatus was withdrawn previously and remains withdrawn. Currently claims 4, 6 and 7 are active and will be examined in this action.

Response to Arguments

Re 103 rejection of claims 4, 6-7 over Larsson et al. and Juarrenz et al.

3. Applicant's arguments filed September 10. 2008 have been fully considered but they are not persuasive. Applicant has amended base claim 4 to add limitation wherein said nucleic acid probe is a DNA fragment or chemically synthesized DNA comprising a nucleic acid sequence complementary to the target nucleic acid. This added limitation does not overcome the cited prior art. Examiner is explaining the rationale below.

In view of the arguments presented by Applicant it is clear that dye YOYO can not be considered as the probe. However Larsson et al. teach use of double

stranded DNA to which the dye binds. One strand of this DNA is the target while the other strand of this DNA is the probe of the instant invention. This interpretation is consistent with the disclosure of the instant application where Applicant uses Poly dA strand as a template and Poly dT strand as complementary strand to make double stranded DNA. The cationic dye is bound to the resulting double stranded DNA.

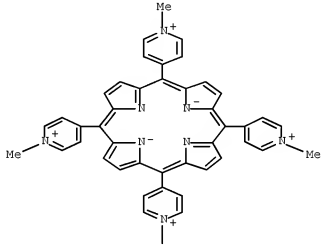
Thus the double stranded DNA taught by Larsson et al. is a product obtained as a result of carrying out a method step of bringing a nucleic acid probe and a sample containing a target nucleic acid into contact with each other under hybridization conditions to form a hybrid nucleic acid composed of said nucleic acid probe and said target nucleic acid. This product meets the limitation wherein said nucleic acid probe is a DNA fragment or chemically synthesized DNA comprising a nucleic acid sequence complementary to the target nucleic acid because said nucleic acid probe is a DNA fragment comprising a nucleic acid sequence complementary to the target nucleic acid.

Thus Larsson et al. teach step (ii) bringing a nucleic acid probe and a sample containing a target nucleic acid into contact with each other under hybridization conditions to form a hybrid nucleic acid composed of said nucleic acid probe and said target nucleic acid, wherein said nucleic acid probe is a DNA fragment or chemically synthesized DNA comprising a nucleic acid sequence complementary to the target nucleic acid.

The cationic dye that can be represented by formula I is taught by Juarrenz et al. This dye binds to DNA and has an inherent property of exhibiting

CD spectra when bound to DNA. In addition Juarrenz et al. teaches that this compound does not intercalate in DNA rather it's an outside binder. Thus art teaches the exact cationic compound TMAP shown below that bind to DNA.

PAGE 1-A



that meets the requirement of a compound depicted by general formula I

(I): X-(Y-Z)n

where n denotes 1 to 12,

X represents a choromophore having at least four pyrrole rings,

Y represents a connecting group or a direct bond between X and Z, and

Z represents a cationic functional group, or a functional group whose property is convertible to a cationic property.

Thus art teaches two cationic compounds that bind to DNA. Larsson et al. teaches CD measurement from DNA bound to YOYO. Porphyrin derivatives taught by Juarrenz et al. are dyes that also bind DNA and have the inherent property of exhibiting CD spectra. Compound TMAP has an inherent property

that it exhibits a CD spectra when bound to DNA. This is evidenced by Seokjoo Hong and Sungho Huh (2003) Bull. Korean Chem Soc. Vol. 24: no. 1 Fig. 3 on page 139 where CD spectra of TMAP is shown at various molar ratios (r) of [porphyrin]/[DNA]. This reference is not being provided to applicant as it is cited in IDS submitted by applicant.

Thus one of ordinary skill can readily use one or the other dye for binding DNA and measuring CD depending on the experimental design and the parameter they are interested in monitoring. See MPEP 2144.06 Art Recognized Equivalence for the Same Purpose

SUBSTITUTING EQUIVALENTS KNOWN FOR THE SAME PURPOSE

In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982).

Applicant's argument regarding disadvantages of using YOYO as a cationic dye are not relevant as Examiner is not using Larsson et al. to teach the cationic compound of formula I recited in claim 4. Juarrenz et al. is teaching the cationic compound of formula I recited in claim 4 as the dye used for CD measurements.

Lastly Applicant is arguing mechanistic differences between how YOYO binds to DNA vs cationic compound of formula I. Applicant is reminded that instant claim language does not recite these mechanisms and thus Applicant is arguing limitations that are not part of recited claims under consideration. Further, results or mechanisms which are inherent in a method do not carry patentable weight.

Therefore previously cited art is still valid and the rejections of claims 4, 6-7 over Larsson et al. and Juarrenz et al. are being maintained.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 4, 6 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Larsson et al. (1994) J. Am. Chem. Soc. 116:8459-8465 further in view of Juarrenz et al. (April 1996) J. of microscopy vol. 182, Pt. 1, pp. 46-49 (provided by Applicant in IDS).

Regarding claim 4, Larsson et al. teach : A method for detecting a hybrid nucleic acid (see line 1 abstract where double stranded DNA is taught. The teaching of double stranded DNA is being interpreted broadly to teach a hybrid nucleic acid—which by definition is double stranded) by use of a cationic dye compound (YOYO), comprising:

Larsson et al. teach use of double stranded DNA to which the dye binds. One strand of this DNA is the target while the other strand of this DNA is the probe of the instant invention. This interpretation is consistent with the disclosure of the instant application where Applicant uses Poly dA strand as a template and Poly dT strand as complementary strand to make double stranded DNA. The cationic dye is bound to the resulting double stranded DNA.

Thus the double stranded DNA taught by Larsson et al. is a product obtained as a result of carrying out a method step of bringing a nucleic acid probe and a sample containing a target nucleic acid into contact with each other under hybridization conditions to form a hybrid nucleic acid composed of said nucleic acid probe and said target nucleic acid. This product meets the limitation wherein said nucleic acid probe is a DNA fragment or chemically synthesized DNA comprising a nucleic acid sequence complementary to the target nucleic

acid because said nucleic acid probe is a DNA fragment comprising a nucleic acid sequence complementary to the target nucleic acid.

binding said cationic dye compound onto said hybrid nucleic acid by adding the cationic dye compound before, during or after said hybridization(see abstract where cationic dye is bound to double stranded (hybrid of instant claims) nucleic acid); and

measuring circular dichroism of said cationic dye compound bound onto said hybrid nucleic acid (see abstract where measurement of circular dichroism (CD) of said cationic dye compound bound onto said hybrid nucleic acid is taught) .

Regarding claim 7, Larsson et al. teach: The method further comprising:

immobilizing an analyte having said target nucleic acid or said nucleic acid probe onto a solid phase carrier to bring said analyte and said nucleic acid probe into contact with each other under hybridization conditions (see page 8459 par 3 where electrophoretic behavior of ds DNA in gels of fluorescently stained DNA is taught. By teaching gel (as solid phase) electrophoresis of double stranded DNA Larsson et al. teach immobilizing an analyte having said target nucleic acid or said nucleic acid probe onto a solid phase carrier to bring said analyte and said nucleic acid probe under hybridization conditions.

Regarding claim 4 Larsson et al. do not teach wherein said cationic dye compound is represented by the following general formula (I): X-(Y-Z)n

where n denotes 1 to 12,

X represents a choromophore having at least four pyrrole rings,

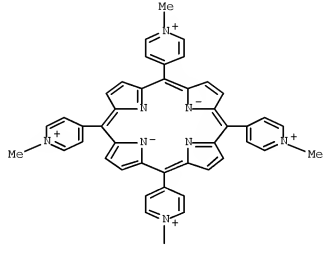
Y represents a connecting group or a direct bond between X and Z, and

Z represents a cationic functional group, or a functional group whose property is convertible to a cationic property.

Regarding claims 4 and 6, Juarrenz et al. teach meso-tetra (4-N-methylpyridyl)porphine (T4MpyP) and meso-tetra (p-N-trimethylanilinium) porphine (TMAP) (see abstract) as a cationic dye compound is represented by the following general formula (I): X-(Y-Z)n. A search done in STN for these chemicals provides following structure.

```
L14   3 ANSWERS   REGISTRY  COPYRIGHT 2007 ACS on STN
IN    Pyridinium, 4,4',4'',4'''-(21H,23H-porphine-5,10,15,20-
tetrayl)tetrakis[1-
      methyl-, bis(inner salt)  (9CI)
MF    C44 H36 N8
```

PAGE 1-A

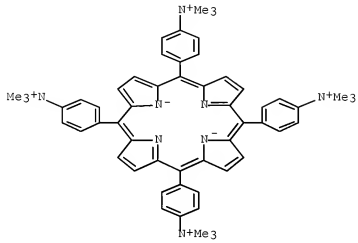


PAGE 2-A

J
Me

```
L14   3 ANSWERS   REGISTRY  COPYRIGHT 2007 ACS on STN
IN    Benzenaminium, 4,4',4'',4'''-(21H,23H-porphine-5,10,15,20-
      tetrayl)tetrakis[N,N,N-trimethyl-, bis(inner salt)  (9CI)
```

MF C56 H60 N8



Thus regarding claim 4, Juarrenz et al. teach wherein said cationic dye compound is represented by the following general formula (I): X-(Y-Z)n

Thus regarding claim 6, Juarrenz et al. teach wherein said choromophore is selected from the group consisting of porphyrin, porphyrin derivatives.

It would have been prima facie obvious to one of ordinary skill in the art to practice the method of Juarrenz et al. in the method of Larsson et al. at the time the invention was made.

Both YOYO taught by Larsson et al. and porphyrin derivatives taught by Juarrenz et al. are dyes that bind to DNA. TMAP is a porphyrin derivative compound of formula I. This compound has an inherent property of exhibiting CD spectra when bound to DNA. In addition Juarrenz et al teaches that this compound does not intercalate in DNA rather it's an outside binder. Thus art teaches two cationic compounds that bind to DNA. Larsson et al. teaches CD

measurement from DNA bound to YOYO. Porphyrin derivatives taught by Juarrenz et al. are dyes that also bind DNA and have the inherent property of exhibiting CD spectra. Thus one of ordinary skill can readily use one or the other dye for binding DNA and measuring CD depending on the experimental design and the parameter they are interested in monitoring. See MPEP 2144.06 Art Recognized Equivalence for the Same Purpose

SUBSTITUTING EQUIVALENTS KNOWN FOR THE SAME PURPOSE

In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982).

Conclusion

7. All claims under consideration 4, 6-7 are rejected over prior art.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUCHIRA PANDE whose telephone number is (571)272-9052. The examiner can normally be reached on 8:30 am -5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637

Suchira Pande
Examiner
Art Unit 1637